

=> d 112 2-4

✓ 5,278,287, Jan. 11, 1994, Human cytokine; \*\*Barrett Rollins\*\*, et al., 530/351; 435/69.1, 69.5, 240.2, 252.3, 320.1; 530/324, 350; 536/23.1, 23.2, 23.5, 23.51, 23.52 [IMAGE AVAILABLE]

✓ 5,212,073, May 18, 1993, Process for producing human JE cytokine; \*\*Barrett Rollins\*\*, et al., 435/69.5, 69.1, 240.2, 252.3, 320.1; 530/324, 350, 351; 536/23.5, 23.52 [IMAGE AVAILABLE]

✓ 5,179,078, Jan. 12, 1993, Method of suppressing tumor formation in vivo; \*\*Barrett Rollins\*\*, et al., 514/2; 435/252.3; 514/12; 530/324, 351 [IMAGE AVAILABLE]

=> d 119 4

✓ 5,458,874, Oct. 17, 1995, Method of increasing \*\*monocyte\*\* chemotaxis with CAP37 and \*\*monocyte\*\* chemotactic portions thereof; Heloise A. Pereira, et al., 424/85.1; 435/212; 514/12, 21 [IMAGE AVAILABLE]

=> d 119 2

✓ 5,484,885, Jan. 16, 1996, Chemotactic, antibiotic and lipopolysaccharide-binding peptide fragments of CAP37; Heloise A. Pereira, et al., 530/326, 328 [IMAGE AVAILABLE]

=> d his

(FILE 'USPAT' ENTERED AT 13:24:02 ON 21 MAY 96)

E YOSHIMURA, TEI/IN

L1 1 S E4

E ROBINSON, ELIZ/IN

L2 3 S E4

E APPELLA, E/IN

E LEONARD, ED/IN

L3 5 S E7

L4 294 S MONOCYT?/TI,AB,CLM

L5 90 S CHEMOTA?/TI,AB,CLM

L6 9 S L4 AND L5

L7 88954 S ACTIVAT?/TI,AB,CLM

L8 53 S L4 AND L7

L9 51 S L8 NOT L6

L10 117948 S ATTRACT?

L11 39 S L4 AND L10

E ROLLINS, BAR/IN

L12 4 S E4

L13 1 S JE (2W) CYTOKIN?

L14 470 S JE

L15 6 S L4 AND L14

L16 271 S CYTOKIN?/TI,AB,CLM  
L17 10 S L16 AND L4  
L18 193 S CHEMOATTR?A?  
L19 13 S L4 AND L18

?t s6/7/1,7-9

6/7/1 (Item 1 from file: 55)  
DIALOG(R)File 55:BIOSIS PREVIEWS(R)  
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7364931 BIOSIS Number: 89015950

IDENTIFICATION OF MONOCYTE CHEMOTACTIC ACTIVITY PRODUCED BY MALIGNANT  
CELLS

✓GRAVES D T; JIANG Y L; WILLIAMSON M J; VALENTE A J  
DEP. ORAL BIOL., BOSTON UNIV. MED. CENTER, BOSTON, MA 02118.  
SCIENCE (WASHINGTON D C) 245 (4925). 1989. 1490-1493. CODEN: SCIEA  
Full Journal Title: SCIENCE (Washington D C)  
Language: ENGLISH

Human malignant cells secrete low molecular size proteins that attract peripheral blood monocytes and may be responsible for the accumulation of tumor-associated macrophages observed in vivo. Similar chemotactic proteins are secreted by cultured vascular smooth muscle cells. The predominant monocyte chemoattractants produced by tumor cells of differing origin were demonstrated to be related to smooth muscle cell-derived chemotactic factor. Thus, a single class of chemotactic proteins is produced by different cell types, which suggests a common mechanism for the recruitment of monocytes and macrophages. These results are significant in view of the potential of macrophages to affect tumor growth.

6/7/7 (Item 7 from file: 55)  
DIALOG(R)File 55:BIOSIS PREVIEWS(R)  
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7067443 BIOSIS Number: 87127964

PURIFICATION AND AMINO ACID ANALYSIS OF TWO HUMAN GLIOMA-DERIVED MONOCYTE  
CHEMOATTRACTANTS

✓YOSHIMURA T; ROBINSON E A; TANAKA S; APPELLA E; KURATSU J-I; LEONARD E J  
IMMUNOPATHOL. SECT., LAB. OF IMMUNOBIOL., NCI, FREDERICK, MD. 21701.  
J EXP MED 169 (4). 1989. 1449-1460. CODEN: JEMEA  
Full Journal Title: Journal of Experimental Medicine  
Language: ENGLISH

Two chemoattractants for human monocytes were purified to apparent homogeneity from the culture supernatant of a glioma cell line (U-105MG) by sequential chromatography on Orange A-Sepharose, an HPLC cation exchanger, and a reverse phase HPLC column. On SDS-PAGE gels under reducing or nonreducing conditions, the molecular masses of the two peptides glioma-derived chemotactic factor 1 and 2 were 15 and 13 kD, respectively. Amino acid composition of these molecules was almost identical, and differed from other cytokines that have been reported. The NH2 terminus of

each peptide was apparently blocked. When tested for chemotactic efficacy, the peptides attracted .apprx. 30% of the monocytes added to chemotaxis chambers, at the optimal concentration of  $10^{-9}$  M. Potency and efficacy were comparable with that of FMLP, which is often used as a reference attractant. The activity was chemotactic rather than chemokinetic. In contrast to their interaction with human monocytes, the pure peptides did not attract neutrophils. These pure tumor-derived chemoattractants can now be compared with attractants produced by normal cells and evaluated for their biological significance in human neoplastic disease.

6/7/8 (Item 8 from file: 55)  
DIALOG(R) File 55:BIOSIS PREVIEWS(R)  
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7065888 BIOSIS Number: 87126409

COMPLETE AMINO ACID SEQUENCE OF A HUMAN MONOCYTE CHEMOATTRACTANT A  
PUTATIVE MEDIATOR OF CELLULAR IMMUNE REACTIONS

ROBINSON E A; YOSHIMURA T; LEONARD E J; TANAKA S; GRIFFIN P R;  
SHABANOWITZ J; HUNT D F; APPELLA E

LAB. CELL BIOLOGY, NATL. CANCER INST., BETHESDA MD. 20892.

✓ PROC NATL ACAD SCI U S A 86 (6). 1989. 1850-1854. CODEN: PNASA

Full Journal Title: Proceedings of the National Academy of Sciences of  
the United States of America

Language: ENGLISH

In a study of the structural basis for leukocyte specificity of chemoattractants, we determined the complete amino acid sequence of human glioma-derived monocyte chemotactic factor (GDCF-2), a peptide that attracts human monocytes but not neutrophils. The choice of a tumor cell product for analysis was dictated by its relative abundance and an amino acid composition indistinguishable from that of lymphocyte-derived chemotactic factor (LDCF), the agonist thought to account for monocyte accumulation in cellular immune reactions. By a combination of Edman degradation and mass spectrometry, it was established that GDCF-2 comprises 76 amino acid residues, commencing at the N terminus with pyroglutamic acid. The peptide contains four half-cystines, at positions 11, 12, 36, and 52, which create a pair of loops, clustered at the disulfide bridges. The relative positions of the half-cystines are almost identical to those of monocyte-derived neutrophil chemotactic factor (MDNCF), a peptide of similar mass but with only 24% sequence identity to GDCF. Thus, GDCF and MDNCF have a similar gross secondary structure because of the loops formed by the clustered disulfides, and their different leukocyte specificities are most likely determined by the large differences in primary sequence.

6/7/9 (Item 9 from file: 55)  
DIALOG(R) File 55:BIOSIS PREVIEWS(R)

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7055139 BIOSIS Number: 87115660

PURIFICATION AND AMINO ACID ANALYSIS OF TWO HUMAN MONOCYTE  
CHEMOATTRACTANTS PRODUCED BY PHYTOHEMAGGLUTININ-STIMULATED HUMAN BLOOD  
MONONUCLEAR LEUKOCYTES

YOSHIMURA T; ROBINSON E A; TANAKA S; APPELLA E; LEONARD E J

IMMUNOPATHOL. SECT., LAB. IMMUNOBIOLOG., NATL. CANCER INST., FREDERICK, MD.  
21701, USA.

✓ IMMUNOL 142 (6). 1989. 1956-1962. CODEN: JOIMA

Full Journal Title: Journal of Immunology

Language: ENGLISH

Physicochemical characteristics of monocyte chemotactic activity in the culture fluid of PHA-stimulated human mononuclear leukocytes (MNL) were investigated. Among several chemotactic activity peaks eluted from a TSK-2000 gel filtration column, one peak, corresponding to a molecular mass of 17 kDa, accounted for about 40% of total chemotactic activity. On a chromatofocusing column, most of the 17-kDa activity eluted in a pH range of 9.4 to 7.9. It could bind to Orange-A Sepharose. These three characteristics-molecular mass, basic isoelectric point, and dye column binding.were similar to those of human glioma-derived monocyte chemotactic factor (GDCF), recently purified in our laboratory. Therefore, the MNL-derived chemoattractant was purified by the same procedures used for purification of GDCF, namely Orange-A Sepharose chromatography, carboxymethyl (CM)-HPLC, and reverse phase (RP) HPLC. About 50% of the culture fluid chemotactic activity bound to Orange-A Sepharose and was eluted in a single peak by a NaCl gradient. The active pool from the Orange-A column was separated into two sharp peaks by CM-HPLC, each of which eluted at identical acetonitrile concentrations from a RP HPLC column. By SDS-PAGE, the peptides had apparent molecular masses of 15 and 13 kDa and appeared homogeneous. Amino acid analysis showed that the composition of the two peptides was almost identical; and the N terminus of each peptide was apparently blocked. Shared characteristics of these peptides and the GDCF peptides include identical elution patterns from CM- and RP HPLC columns, identical SDS-PAGE migration, almost identical amino acid composition, and blocked N terminus. This suggests that the monocyte attractants isolated from culture fluid of PHA-stimulated MNL are identical to those derived from human glioma cells.

?t s12/7/4,15,24

12/7/4 (Item 4 from file: 55)

DIALOG(R)File 55:BIOSIS PREVIEWS(R)

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7363444 BIOSIS Number: 89014463

THE HUMAN HOMOLOG OF THE JE GENE ENCODES A MONOCYTE SECRETORY PROTEIN

ROLLINS B J; STIER P; ERNST T; WONG G G

DIV. MED., DANA-FARBER CANCER INST., HARVARD MED. SCH., BOSTON, MASS.

02115.

MOL CELL BIOL 9 (11). 1989. 4687-4695. CODEN: MCEBD

Full Journal Title: Molecular and Cellular Biology

Language: ENGLISH

The mouse fibroblast gene, JE, was one of the first platelet-derived growth factor-inducible genes to be described as such. The protein encoded by JE (mJE) is the prototype of a large family of secreted, cytokinelike glycoproteins, all of whose members are induced by a mitogenic or activation signal in monocytes, macrophages, and T lymphocytes; JE is the only member to have been identified in fibroblasts. We report the identification of a human homolog for murine JE, cloned from human fibroblasts. The protein predicted by the coding sequence of human JE (hJE) is 55 amino acids shorter than mJE, and its sequence is identical to that of a recently purified monocyte chemoattractant. When expressed in COS cells, the human JE cDNA directed the secretion of N-glycosylated proteins of Mr 16,000 to 18,000 as well as proteins of Mr 15,500, 15,000, and 13,000. Antibodies raised against mJE recognized these hJE species, all of which were secreted by human fibroblasts. hJE expression was stimulated in HL60 cells during phorbol myristate acetate-induced monocytoid differentiation. However, resting human monocytes constitutively secreted hJE; treatment with gamma interferon did not enhance hJE expression in monocytes, and treatment with phorbol myristate acetate or lipopolysaccharide inhibited its expression. Thus, human JE encodes yet another member of the large family of JE-related cytokinelike proteins, in this case a novel human monocyte and fibroblast secretory protein.

12/7/15 (Item 15 from file: 55)

DIALOG(R)File 55:BIOSIS PREVIEWS(R)

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7056520 BIOSIS Number: 87117041

PRODUCTION AND CHARACTERIZATION OF HUMAN GLIOMA CELL-DERIVED MONOCYTE CHEMOTACTIC FACTOR

KURATSU J-I; LEONARD E J; YOSHIMURA T

*applicants*

IMMUNOPATHOL. SECT., LAB. IMMUNOBIOL., NATL. CANCER INST., FREDERICK, MD.

21701.

J NATL CANCER INST (BETHESDA) 81 (5). 1989. 347-351. CODEN: JNCIE

Full Journal Title: Journal of the National Cancer Institute (Bethesda)

Language: ENGLISH

Since infiltration of monocytes into tumors may be mediated by tumor-derived chemoattractants, we characterized the monocyte-chemotactic activity (MCA) produced by glioma cell lines. The amount of MCA in the culture fluid of five lines tested differed by a factor of 25. U-105MG, the best producer, was selected for further study. After cells reached

confluence and the medium was changed, MCA was detected by day 3 and remained at comparable levels on days 4 and 5. The molecular mass of MCA was approximately 17 kilodaltons, and the estimated isoelectric point ranged between pI 7 and pI 9. Because of the high constitutive production of MCA by U-105MG, sufficient material can be obtained for complete chemical characterization of this mediator of inflammation.

12/7/24 (Item 24 from file: 55)  
DIALOG(R)File 55:BIOSIS PREVIEWS(R)  
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6796003 BIOSIS Number: 36126524

INITIAL CHARACTERIZATION OF MONOCYTE CHEMOATTRACTANT

✓ GRAVES D T; JIANG Y L; VALENTE A J

BOSTON UNIV. SCH. GRADUATE DENTISTRY, BOSTON, MASS.

18TH ANNUAL SESSION OF THE AMERICAN ASSOCIATION FOR DENTAL RESEARCH, SAN FRANCISCO, CALIFORNIA, USA, MARCH 15-19, 1989. J DENT RES 68 (SPEC. ISSUE). 1989. 352. CODEN: JDREA

Language: ENGLISH

?t s16/7/2,12

16/7/2 (Item 2 from file: 55)  
DIALOG(R)File 55:BIOSIS PREVIEWS(R)  
(c) 1996 BIOSIS. All rts. reserv.

7043475 BIOSIS Number: 87103996

CLONING AND SEQUENCING OF THE COMPLEMENTARY DNA FOR HUMAN MONOCYTE CHEMOTACTIC AND ACTIVATING FACTOR MCAF

FURUTANI Y; NOMURA H; NOTAKE M; OYAMADA Y; FUKUI T; YAMADA M; LARSEN C G; OPPENHEIM J J; MATSUSHIMA K

RES. LAB., DAINIPPON PHARMACEUTICAL CO. LTD., ENOKI-CHO 33-94, SUITA/OSAKA 546, JPN.

BIOCHEM BIOPHYS RES COMMUN 159 (1). 1989. 249-255. CODEN: BBRCA

Full Journal Title: Biochemical and Biophysical Research Communications

Language: ENGLISH

cDNA clones having a nucleotide sequence encoding a human monocyte chemotactic and activating factor (MCAF) were isolated and sequenced. The amino acid sequence deduced from the nucleotide sequence reveals the primary structure of the MCAF precursor to be composed of a putative signal peptide sequence of 23 amino acid residues and a mature MCAF sequence of 76 amino acid residues. The amino acid sequence of MCAF showed 25-55% homology with other members of an inducible cytokine family, including macrophage inflammatory protein and some putative polypeptide mediators known as JE, LD78, RANTES and TCA-3. This suggests that MCAF is a member of family of factors involved in immune and inflammatory responses.

16/7/12 (Item 1 from file: 72)  
DIALOG(R) File 72:EMBASE  
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7553699 EMBASE No: 89275981

The human homolog of the JE gene encodes a monocyte secretory protein  
Rollins B.J.; Stier P.; Ernst T.; Wong G.G.  
Division of Medicine, Dana-Farber Cancer Institute, Harvard Medical  
School, Boston, MA 02115 USA

MOL. CELL. BIOL. (USA) , 1989, 9/11 (4687-4695) CODEN: MCEBD ISSN:  
0270-7306

LANGUAGES: English  
?ds

Set	Items	Description
S1	7789968	PY=1990:1996
S2	61359	MONOCYTE?/TI,AB
S3	24063	S2 NOT S1
S4	28215	ATTRACT?/TI,AB
S5	163	S3 AND S4
S6	76	RD (unique items)
S7	624469	ACTIVAT?/TI,AB
S8	6023	S3 AND S7
S9	6742	CHEMOATTRAC?/TI,AB
S10	315	S3 AND S9
S11	270	S10 NOT S5
S12	139	RD (unique items)
S13	1757	JE/TI,AB
S14	26	S3 AND S13
S15	21	S14 NOT (S5 OR S11)
S16	13	RD (unique items)
S17	27467	CHEMOTA?/TI,AB
S18	1341	S3 AND S17

?logout

21may96 12:51:10 User214483 Session D503.2  
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\$0.00 144 Type(s) in Format 6  
\$10.80 8 Type(s) in Format 7  
\$10.80 152 Types  
\$14.94 Estimated cost File55  
\$1.71 0.057 Hrs File154  
\$0.00 61 Type(s) in Format 6  
\$0.00 61 Types



\$1.71 Estimated cost File154  
\$5.04 0.056 Hrs File72  
\$0.00 23 Type(s) in Format 6  
\$1.45 1 Type(s) in Format 7  
\$1.45 24 Types  
\$6.49 Estimated cost File72